**REMARKS**

Claims 8, 9, 13-15, 17-19 and 21-33 are pending in the instant application. Claims 8, 9, 13-15, 17-19 and 21-33 have been rejected. Claims 8, 13, 14, 17, 18, 21, 23 and 26 have been amended. Claims 22 and 25 have been canceled. New claims 34-45 have been added. Support for these amendments is provided in the specification at page 4, lines 26-28, page 7, line 34 through page 8, line 2, page 8, lines 11-17 and the Sequence Listing. No new matter is added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

**I. Objection to Claims 13, 17, 21, 22-24, 26 and 27**

Claims 13, 17, 21, 22-24, 26 and 27 have been objected to as being dependent claims which do not further limit the base claim from which they depend. Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have canceled claim 22. Applicants have amended claims 13, 17, and 21 to state that the native protein encoded by SEQ ID NO:1 comprises amino acids 14 to 327 of SEQ ID NO:2. Further Applicants have amended claims 23 and 26 to clarify that the monoclonal or polyclonal antibody binds to the active protease domain of the native protein.

Support for these amendments is provided in teachings of the instant specification relating to characteristics of SEQ ID NO:1 and SEQ ID NO:2 and what was well known in the art at the time of filing the instant application. These amendments now render the dependent claims further limiting with respect to the base claim from which they depend.

Withdrawal of this objection is therefore respectfully requested.

**II. Rejection of Claims 8, 9, 13-15, 17-19 and 21-33 under 35 U.S.C. 112, first paragraph**

Claims 8, 9 and 13-15, 17-19 and 21-33 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The Examiner suggests that the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants argument that Pro104 is the same as testisin, confirmed in post-filing date publications of Tang et al. and Papkoff to be overexpressed in ovarian cancer, were deemed unpersuasive by the Examiner as the

Examiner suggests that Pro104 (limited to the SEQ ID NO:2 protein) is not the same as testisin.

Applicants respectfully traverse this rejection.

SEQ ID NO:2 of the instant application is a polypeptide containing the deduced amino acid sequence of the polynucleotide SEQ ID NO:1 and depicts in its sequence 13 amino acids before the initial methionine of the native protein encoded by SEQ ID NO:1. These 13 deduced amino acids depicted in SEQ ID NO:2 occur prior to the translation initiation codon and thus do not occur in the native protein encoded by SEQ ID NO:1. It is these 13 deduced amino acids in SEQ ID NO:2 which result in the Examiner's suggestion that "instant SEQ ID NO:2 is not the same as testisin". However, comparison of the native protein encoded by SEQ ID NO:1, depicted in SEQ ID NO:2 from the first methionine at amino acid position 14 to position 327, with testisin shows the proteins to be identical.

Accordingly in an earnest effort to advance the prosecution of this case, Applicants have amended the claims in accordance with teachings in the specification at page 4, lines 26-28, and page 7, line 34 through page 8,

line 2, to state and antibody which specifically binds native protein encoded by SEQ ID NO:1.

The native protein encoded by SEQ ID NO:1, testisin, antibodies thereto and methods of using these antibodies to image a gynecologic cancer are clearly enabled by the instant specification.

The test of enablement is whether one reasonably skilled in the art could make or use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation. See MPEP 2164.01. Thus, the test of enablement is not whether any experimentation is necessary but whether, if experimentation is necessary it is undue. In re Angstadt, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). If the art typically engages in such experimentation, it is not considered undue. See In re Certain Limited-Charge Cell Culture Microcarriers, 221 USPQ 1165, 1174 ((Int'l Trade Comm'n 1983), aff'd sub nom., Massachusetts Institute of Technology v. A.B. Fortia, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985).

Any experimentation necessary to make and use the invention as claimed was routine to the skilled artisan

when coupled with the information taught in the specification. In particular, protein sequences and/or open reading frames were routinely obtained by those skilled in the art at the time of filing the instant patent application based upon information such as provided in the instant specification. In particular, the specification teaches in Examples 1 and 2 that polynucleotide SEQ ID NO:1 is based on an mRNA molecule and thus has a set 5' to 3' orientation. See in particular pages 16-18 of the instant specification. From this information, one skilled in the art would know that the native protein is encoded in the forward (5' to 3') direction of SEQ ID NO:1. This characteristic taught in the originally filed specification limits the potential frame translations to three possibilities.

Applicants are also providing in a Supplemental IDS submitted herewith evidence of multiple tools available by 1998, thus preceding the September 23, 1998 priority date of the instant application, which were routinely used to determine the native protein sequence encoded by and/or the open reading frame of a polynucleotide such as SEQ ID NO:1

based solely upon the information provided in the instant specification and what was known in the art.

In addition to these methods which identify potential open reading frames from a polynucleotide sequence, also known as of the filing date of the instant application was that the sequence flanking a functional initiator codon in eukaryotic mRNA sequences is a non-random sequence. The most frequently occurring sequence is referred to as the Kozak consensus sequence (see Kozak, M. Nucleic Acids Research 1981 9(20):52335262; Kozak, M. Nucleic Acids Research 1984 12(2):857-872; and Kozak, M. Nucleic Acids Research 1987 15(20):8125-8148; copies of these references are submitted in the Supplemental Information Disclosure Statement being filed herewith.

Because the sequence and expression data of SEQ ID NO:1 was based on an mRNA molecule, one of ordinary skill would know the correct orientation to be 5′-3′. Given the orientation, one of ordinary skill could readily scan the entirety of SEQ ID NO: 1 examining any of the three possible frames for a start codon identified by the Kozak consensus sequence. The first ATG start codon in frame 1 and the flanking sequence, GAGGCCATGG, meets the

requirements for an initiator codon as identified by the Kozak eukaryotic sequence.

Also known as of the filing date of the instant application was that the 5'-proximal ATG serves as the initiator codon for the majority of mRNAs (see Kozak, M. Nucleic Acids Research 1984 12(2):857-872; Singer, M. and Berg, P. Genes & Genomes 1991 University Science Books (Mill Valley, CA), pages 180-182; and Watson et al. Molecular Biology of the Gene 1987 The Benjamin/Cummings Publishing Company, Inc. (Menlo Park, CA), pages 568-569; copies of these references are submitted in the Supplemental Information Disclosure Statement being filed herewith).

Accordingly, one of skill in the art could routinely identify the start codon for SEQ ID NO:1 and the native protein encoded thereby, in this case testisin, based upon teachings of the instant specification and what was well known in the art at the time of filing the instant application.

Also well known and routine to those of skill in the art at the time of filing the instant application were methods for expressing native protein encoded by a nucleotide sequence such as SEQ ID NO:1 and generating antibodies thereto.

Information well known in the art does not need to be described in detail in the specification. MPEP 2163 at page 2100-170 and Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986).

Accordingly reconsideration of the confirming evidence of Tang et al. and Papkoff et al., which, contrary to the Examiner's suggestion, are germane to the instant claimed invention is respectfully requested.

Papkoff et al. and Tang et al., clearly confirm teachings in the instant specification, for example at page 7-8 that native protein encoded by SEQ ID NO:1 is over-expressed in a gynecologic cancer. Further, these references confirm that this protein is an antibody target for a gynecologic cancer in accordance with teachings at page 14-16 of the instant specification. Thus, these references confirm that the instant specification teaches one of skill in the art how to make and use the invention as set forth in the instant claims and remove any reason whatsoever to reasonably doubt such teachings. Accordingly, the instant specification meets the requirements of 35 U.S.C. 112, first paragraph.

Withdrawal of this rejection under 35 U.S.C. 112, first paragraph is therefore respectfully requested.

**III. Conclusion**

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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